

Application No.: 10/540,348

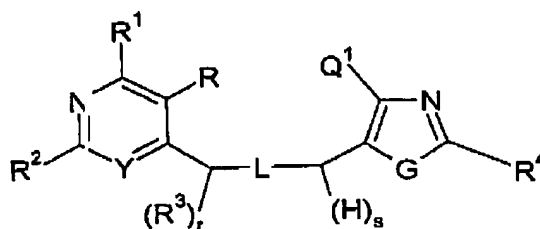
3 of 10

In the Claims

The listing of claims will replace all prior versions and listings of claims in the application.

Listings of claims

1. (amended) A compound of the Formula I:



Formula I

wherein:

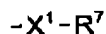
-L- represents a double bond and r and s each represent 1 or 0; or -L- represents a triple bond and r and s each represent 0;

G is selected from O, S and NR⁵;

Y is selected from N and CR⁶;

Q¹ is selected from aryl and heteroaryl,

and wherein Q¹ is optionally substituted by one or more substituents, which may be the same or different, selected from halogeno, trifluoromethyl, trifluoromethoxy, cyano, nitro, hydroxy, amino, carboxy, carbamoyl, (1-6C)alkyl, (2-8C)alkenyl, (2-8C)alkynyl, (1-6C)alkoxy, (2-6C)alkenyloxy, (2-6C)alkynylloxy, (1-6C)alkylthio, (1-6C)alkylsulfosulfinyl, (1-6C)alkylsulfosulfonyl, (1-6C)alkylamino, di-[(1-6C)alkyl]amino, (1-6C)alkoxycarbonyl, N-(1-6C)alkylcarbamoyl, N,N-di-[(1-6C)alkyl]carbamoyl, (2-6C)alkanoyl, (2-6C)alkanoyloxy, (2-6C)alkanoylamino, N-(1-6C)alkyl-(2-6C)alkanoylamino, (3-6C)alkenoylamino, N-(1-6C)alkyl-(3-6C)alkenoylamino, (3-6C)alkynoylamino, N-(1-6C)alkyl-(3-6C)alkynoylamino, N-(1-6C)alkylsulfosulfamoyl, N,N-di-[(1-6C)alkyl]sulfosulfamoyl, (1-6C)alkanesulfosulfonylamino, N-(1-6C)alkyl-(1-6C)alkanesulfosulfonylamino, from a group of the formula:



wherein X¹ is a direct bond or is selected from O and N(R⁸), wherein R⁸ is hydrogen or (1-6C)alkyl, and R⁷ is halogeno-, (1-6C)alkyl, hydroxy-(1-6C)alkyl, (1-6C)alkoxy-(1-6C)alkyl, cyano-(1-6C)alkyl, amino-(1-6C)alkyl, (1-6C)alkylamino-(1-6C)alkyl or di-[(1-6C)alkyl]amino-(1-6C)alkyl, and from a group of the formula :

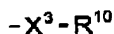


wherein X² is a direct bond or is selected from O, S, SO, SO₂, N(R⁹), CO, CH(OR⁹), CON(R⁹), N(R⁹)CO, N(R⁹)CCN(R⁹), SO₂N(R⁹), N(R⁹)SO₂, C(R⁹)₂O, C(R⁹)₂S and N(R⁹)C(R⁹)₂,

Application No.: 10/540,348

4 of 10

wherein R^9 is hydrogen or (1-6C)alkyl, and Q^2 is aryl, aryl-(1-6C)alkyl, heteroaryl, heteroaryl-(1-6C)alkyl, heterocyclyl or heterocyclyl-(1-6C)alkyl which optionally bears 1, 2 or 3 substituents, which may be the same or different, selected from trifluoromethyl, trifluoromethoxy, cyano, nitro, hydroxy, amino, carboxy, carbamoyl, (1-6C)alkyl, (2-8C)alkenyl, (2-8C)alkynyl, (1-6C)alkoxy, (2-6C)alkenyloxy, (2-6C)alkynyloxy, (1-6C)alkylthio, (1-6C)alkylsulfanyl, (1-6C)alkylsulfonyl, (1-6C)alkylamino, di-[(1-6C)alkyl]amino, (1-6C)alkoxycarbonyl, N-(1-6C)alkylcarbamoyl, N,N-di-[(1-6C)alkyl]carbamoyl, (2-6C)alkanoyl, (2-6C)alkanoyloxy, (2-6C)alkanoylamino, N-(1-6C)alkyl-(2-6C)alkanoylamino, N-(1-6C)alkylsulfamoyl, N,N-di-[(1-6C)alkyl]sulfamoyl, (1-6C)alkanesulfonylamino and N-(1-6C)alkyl-(1-6C)alkanesulfonylamino, or from a group of the formula:



wherein X^3 is a direct bond or is selected from O and $N(R^{11})$, wherein R^{11} is hydrogen or (1-6C)alkyl, and R^{10} is halogeno-(1-6C)alkyl, hydroxy-(1-6C)alkyl, (1-6C)alkoxy-(1-6C)alkyl, cyano-(1-6C)alkyl, amino-(1-6C)alkyl, (1-6C)alkylamino-(1-6C)alkyl or di-[(1-6C)alkyl]amino-(1-6C)alkyl,

and any heterocyclyl group within Q^2 optionally bears 1 or 2 oxo or thioxo substituents;

R is selected from hydrogen, amino, hydroxy, halogeno, (1-6C)alkyl, (1-6C)alkoxy, (1-6C)alkylamino, di-[(1-6C)alkyl]amino, carboxy, (1-6C)alkoxycarbonyl and *N*-(heterocyclyl(3-8C)cycloalkyl)carbamoyl;

R^1 is selected from hydrogen, halogeno, trifluoromethyl, trifluoromethoxy, cyano, nitro, hydroxy, amino, mercapto, carbamoyl, (1-6C)alkyl, (2-8C)alkenyl, (2-8C)alkynyl, (1-6C)alkoxy, (2-6C)alkenyloxy, (2-6C)alkynyloxy, (1-6C)alkylthio, (1-6C)alkylsulfanyl, (1-6C)alkylsulfonyl, (1-6C)alkylamino, di-[(1-6C)alkyl]amino, (1-6C)alkoxycarbonyl, N-(1-6C)alkylcarbamoyl, N,N-di-[(1-6C)alkyl]carbamoyl, (2-6C)alkanoyl, (2-6C)alkanoyloxy, (2-6C)alkanoylamino, N-(1-6C)alkyl-(2-6C)alkanoylamino, (3-6C)alkenoylamino, N-(1-6C)alkyl-(3-6C)alkenoylamino, (3-6C)alkynoylamino, N-(1-6C)alkyl-(3-6C)alkynoylamino, N-(1-6C)alkylsulfamoyl, N,N-di-[(1-6C)alkyl]sulfamoyl, (1-6C)alkanesulfonylamino and N-(1-6C)alkyl-(1-6C)alkanesulfonylamino;

R^2 is selected from hydrogen, halogeno, amino, hydroxy, halogeno, (1-6C)alkyl, (1-6C)alkoxy, (1-6C)alkylthio, (1-6C)alkylamino, di-[(1-6C)alkyl]amino, aryl(1-6C)alkylamino, arylamino, heterocyclyl and (2-6C)alkanoylamino;

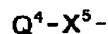
R^3 is selected from hydrogen, (1-6C)alkyl, hydroxy(1-6C)alkyl, carboxy, (1-6C)alkoxycarbonyl, carbamoyl, N-(1-6C)alkylcarbamoyl, N,N-di-[(1-6C)alkyl]carbamoyl and *N*-(heterocyclyl(3-8C)cycloalkyl)carbamoyl;

Application No.: 10/540,348

5 of 10

R^5 is, independently, as defined for R^4 and R^6 , provided that R^5 is not halogeno;

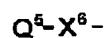
R^4 and R^6 which may be the same or different, are selected from hydrogen, halogeno, trifluoromethyl, trifluoromethoxy, cyano, isocyano, nitro, hydroxy, mercapto, amino, formyl, carboxy, carbamoyl, sulfamoyl, (1-6C)alkyl, (2-8C)alkenyl, (2-8C)alkynyl, (1-6C)alkoxy, (2-6C)alkenyloxy, (2-6C)alkynyloxy, (1-6C)alkylthio, (1-6C)alkylsulfinyl, (1-6C)alkylsulfonyl, (1-6C)alkylamino, di-[(1-6C)alkyl]amino, (1-6C)alkoxycarbonyl, N-(1-6C)alkylcarbamoyl, N,N-di-[(1-6C)alkyl]carbamoyl, (2-6C)alkanoyl, (2-6C)alkanoyloxy, (2-6C)alkanoylamino, N-(1-6C)alkyl-(2-6C)alkanoylamino, (3-6C)alkenoylamino, N-(1-6C)alkyl-(3-6C)alkenoylamino, (3-6C)alkynoylamino, N-(1-6C)alkyl-(3-6C)alkynoylamino, N-(1-6C)alkylsulfamoyl, N,N-di-[(1-6C)alkyl]sulfamoyl, (1-6C)alkanesulfonylamino and N-(1-6C)alkyl-(1-6C)alkanesulfonylamino, or from a group of the formula :



wherein X^5 is a direct bond or is selected from O, S, SO, SO₂, N(R¹²), CO, CH(OR¹²), CON(R¹²), N(R¹²)CO, SO₂N(R¹²), N(R¹²)SO₂, OC(R¹²)₂, SC(R¹²)₂ and N(R¹²)C(R¹²)₂, wherein R¹² is hydrogen or (1-6C)alkyl, and Q^4 is aryl, aryl-(1-6C)alkyl, (3-7C)cycloalkyl, (3-7C)cycloalkyl-(1-6C)alkyl, (3-7C)cycloalkenyl, (3-7C)cycloalkenyl-(1-6C)alkyl, heteroaryl, heteroaryl-(1-6C)alkyl, heterocyclyl or heterocyclyl-(1-6C)alkyl,

and wherein adjacent carbon atoms in any (2-6C)alkylene chain within an R^4 , R^5 or R^6 substituent are optionally separated by the insertion into the chain of a group selected from O, S, SO, SO₂, N(R¹³), CO, CH(OR¹³), CON(R¹³), N(R¹³)CO, SO₂N(R¹³), N(R¹³)SO₂, CH=CH and C≡C wherein R¹³ is hydrogen or (1-6C)alkyl,

and wherein any CH₂=CH- or HC≡C- group within an R^4 , R^5 or R^6 substituent optionally bears at the terminal CH₂= or HC≡ position a substituent selected from halogeno, carboxy, carbamoyl, (1-6C)alkoxycarbonyl, N-(1-6C)alkylcarbamoyl, N,N-di-[(1-6C)alkyl]carbamoyl, amino-(1-6C)alkyl, (1-6C)alkylamino-(1-6C)alkyl and di-[(1-6C)alkyl]amino-(1-6C)alkyl or from a group of the formula :



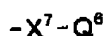
wherein X^6 is a direct bond or is selected from CO and N(R¹⁴)CO, wherein R¹⁴ is hydrogen or (1-6C)alkyl, and Q^6 is aryl, aryl-(1-6C)alkyl, heteroaryl, heteroaryl-(1-6C)alkyl, heterocyclyl or heterocyclyl-(1-6C)alkyl,

and wherein any CH₂ or CH₃ group within a R^4 , R^5 or R^6 substituent optionally bears on each said CH₂ or CH₃ group one or more halogeno or (1-6C)alkyl substituents or a substituent selected from hydroxy, cyano, amino, carboxy, carbamoyl, (1-6C)alkoxy, (1-

Application No.: 10/540,348

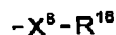
6 of 10

6C)alkylthio, (1-6C)alkylsulfinyl, (1-6C)alkylsulfonyl, (1-6C)alkylamino, di-[(1-6C)alkyl]amino, (1-6C)alkoxycarbonyl, N-(1-6C)alkylcarbamoyl, N,N-di-[(1-6C)alkyl]carbamoyl, (2-6C)alkanoyl, (2-6C)alkanoyloxy, (2-6C)alkanoylamino, N-(1-6C)alkyl-(2-6C)alkanoylamino, N-(1-6C)alkylsulfamoyl, N,N-di-[(1-6C)alkyl]sulfamoyl, (1-6C)alkanesulfonylamino and N-(1-6C)alkyl-(1-6C)alkanesulfonylamino, or from a group of the formula :

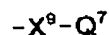


wherein X^7 is a direct bond or is selected from O, S, SO, SO_2 , $N(R^{15})$, CO, $CH(OR^{15})$, $CON(R^{15})$, $N(R^{15})CO$, $SO_2N(R^{15})$, $N(R^{15})SO_2$, $C(R^{15})_2O$, $C(R^{15})_2S$ and $N(R^{15})C(R^{15})_2$, wherein R^{15} is hydrogen or (1-6C)alkyl, and Q^6 is aryl, aryl-(1-6C)alkyl, (3-7C)cycloalkyl, (3-7C)cycloalkyl-(1-6C)alkyl, (3-7C)cycloalkenyl, (3-7C)cycloalkenyl-(1-6C)alkyl, heteroaryl, heteroaryl-(1-6C)alkyl, heterocyclyl or heterocyclyl-(1-6C)alkyl,

and wherein any aryl, heteroaryl, heterocyclyl, cycloalkyl or cycloalkenyl group within a substituent on R^4 , R^5 or R^6 optionally bears 1 or more substituents, which may be the same or different, selected from halogeno, trifluoromethyl, trifluoromethoxy, cyano, nitro, hydroxy, amino, carboxy, carbamoyl, (1-6C)alkyl, (2-8C)alkenyl, (2-8C)alkynyl, (1-6C)alkoxy, (2-6C)alkenyloxy, (2-6C)alkynyloxy, (1-6C)alkylthio, (1-6C)alkylsulfinyl, (1-6C)alkylsulfonyl, (1-6C)alkylamino, di-[(1-6C)alkyl]amino, (1-6C)alkoxycarbonyl, N-(1-6C)alkylcarbamoyl, N,N-di-[(1-6C)alkyl]carbamoyl, (2-6C)alkanoyl, (2-6C)alkanoyloxy, (2-6C)alkanoylamino, N-(1-6C)alkyl-(2-6C)alkanoylamino, N-(1-6C)alkylsulfamoyl, N,N-di-[(1-6C)alkyl]sulfamoyl, (1-6C)alkanesulfonylamino, N-(1-6C)alkyl-(1-6C)alkanesulfonylamino, from a group of the formula :



wherein X^8 is a direct bond or is selected from O and $N(R^{17})$, wherein R^{17} is hydrogen or (1-6C)alkyl, and R^{16} is halogeno-(1-6C)alkyl, hydroxy-(1-6C)alkyl, (1-6C)alkoxy-(1-6C)alkyl, cyano-(1-6C)alkyl, amino-(1-6C)alkyl, (1-6C)alkylamino-(1-6C)alkyl, di-[(1-6C)alkyl]amino-(1-6C)alkyl, (2-6C)alkanoylamino-(1-6C)alkyl or (1-6C)alkoxycarbonylamino-(1-6C)alkyl, and from a group of the formula :



wherein X^9 is a direct bond or is selected from O, S, SO, SO_2 , $N(R^{18})$, CO, $CH(OR^{18})$, $CON(R^{18})$, $N(R^{18})CO$, $SO_2N(R^{18})$, $N(R^{18})SO_2$, $C(R^{18})_2O$, $C(R^{18})_2S$ and $N(R^{18})C(R^{18})_2$, wherein R^{18} is hydrogen or (1-6C)alkyl, and Q^7 is aryl, aryl-(1-6C)alkyl, (3-7C)cycloalkyl, (3-7C)cycloalkyl-(1-6C)alkyl, (3-7C)cycloalkenyl, (3-7C)cycloalkenyl-(1-6C)alkyl, heteroaryl, heteroaryl-(1-6C)alkyl, heterocyclyl or heterocyclyl-(1-6C)alkyl which optionally bears 1 or 2 substituents, which may be the same or different, selected from halogeno, trifluoromethyl, trifluoromethoxy, cyano, nitro, hydroxy, amino, carboxy, carbamoyl, (1-6C)alkyl, (2-

Application No.: 10/540,348

7 of 10

8C)alkenyl, (2-8C)alkynyl, (1-6C)alkoxy, (2-6C)alkenyloxy, (2-6C)alkynyloxy, (1-6C)alkylthio, (1-6C)alkylsulfinyl, (1-6C)alkylsulfonyl, (1-6C)alkylamino, di-[(1-6C)alkyl]amino, (1-6C)alkoxycarbonyl, N-(1-6C)alkylcarbamoyl, N,N-di-[(1-6C)alkyl]carbamoyl, (2-6C)alkanoyl, (2-6C)alkanoyloxy, (2-6C)alkanoylamino, N-(1-6C)alkyl-(2-6C)alkanoylamino, N-(1-6C)alkylsulfamoyl, N,N-di-[(1-6C)alkyl]sulfamoyl, (1-6C)alkanesulfonylamino and N-(1-6C)alkyl-(1-6C)alkanesulfonylamino,

or when G is NR⁶, R⁴ and R⁵ together with the atoms to which they are attached form a fused 5- or 6- membered heteroaryl or heterocyclyl ring, and wherein said fused 5- or 6-membered ring optionally bears one or more substituents as defined for R⁴,

and any fused 5- or 6- membered heterocyclyl ring so formed optionally bears 1 or 2 oxo or thiooxo substituents,

and wherein any heterocyclyl group within any R⁴, R⁵ or R⁶ substituent optionally bears 1 or 2 oxo or thiooxo substituents;

or a pharmaceutically-acceptable salt thereof;

provided the compound is not 4-[2-(6-phenylimidazo[2,1-b][1,3-thiazol-5-yl)ethenyl]-2-pyrimidinamine.

2. (original) A pharmaceutical composition which comprises a compound of the Formula 1, or a pharmaceutically acceptable salt thereof, as defined in claim 1 in association with a pharmaceutically-acceptable diluent or carrier.

3. (canceled)

4. (canceled)

5. (canceled)

6. (new) A compound according to Claim 1 wherein R is selected from hydrogen, halogeno, carboxy, (1-6C)alkoxycarbonyl and *N*-(heterocyclyl(3-8C)cycloalkyl)carbamoyl or a pharmaceutically acceptable salt thereof.

7. (new) A compound according to Claim 1 wherein R¹ is selected from hydrogen, amino and (1-6C)alkyl or a pharmaceutically acceptable salt thereof.

Application No.: 10/540,348

8 of 10

8. (new) A compound according to Claim 1 wherein R^2 is selected from hydrogen, halogeno, hydroxy, amino, (1-6C)alkylthio, (1-6C)alkylamino, di-[(1-6C)alkyl]amino, aryl(1-6C)alkylamino, arylamino, heterocyclyl and (2-6C)alkanoylamino or a pharmaceutically acceptable salt thereof.
9. (new) A compound according to Claim 1 wherein R^3 is selected from hydrogen, carboxy, (1-6C)alkoxycarbonyl, hydroxy(1-6C)alkyl, N-(1-6C)alkylcarbamoyl and N-(heterocyclyl(3-8C)cycloalkyl)carbamoyl or a pharmaceutically acceptable salt thereof.
10. (new) A compound according to Claim 1 wherein R^4 is hydrogen and R^5 is selected from (1-6C)alkyl, aryl(1-6C)alkyl, carboxy(1-6C)alkyl, heterocyclyl(1-6C)alkyl and amino(1-6C)alkyl wherein the amino group is optionally substituted by one or more (1-6C)alkyl or a pharmaceutically acceptable salt thereof.
11. (new) A method of inhibiting a Tie2 receptor tyrosine kinase in a warm-blooded animal in need of such treatment, comprising administering to said animal an effective amount of a compound of the formula I, or a pharmaceutically acceptable salt thereof, as defined in claim 1.
12. (new) A method of producing an anti-angiogenic effect in a warm-blooded animal, in need of such treatment, comprising administering to said animal an effective amount of a compound of the formula I, or a pharmaceutically acceptable salt thereof, as defined in claim 1.